990-34 Postischemic Myocardial Contractile Dysfunction in the Double Heart Model. Role of Catecholamines

T.M. Frank, V. Stangl, R. Kaestner, T. Berndt, H. Hess, S.B. Felix, G. Baumann. *Charité, Humboldt-Universität, Berlin, Germany*

We have previously reported that after global ischemia (IS) cardiodepressive mediators are released during reperfusion. In the present study, we investigated whether the cardiodepressive effects of these mediators depend on the duration of IS. Particular interest was focussed on the modulating effects of myocardial catecholamines (C) during reperfusion. Two isolated guinea pig hearts were serially perfused by the Langendorff technique at constant flow (10 ml/min) with a modified Krebs-Henseleit-solution. The coronary effluent (CE) of the first heart (H1) was collected, reoxygenized and rapidly transported to the second heart (H2). After 10 min IS of H1 (n = 6) serial perfusion induced a reversible decrease of left ventricular systolic pressure (LVSP) (basal 69 ± 5 mmHg, SEM) by 20%, +LVdP/dt_{max} (basal 1592 ± 77 mmHg/s) by 46%, −LVdP/dt_{max} (basal 1370 ± 117 mmHg/s) by 43% and coronary perfusion pressure (CPP) (basal 86 ± 6 cmH_2O) by 23% in H2. However, after 30 min IS of H1 (n = 5) LVSP, +LVdP/dt_{max}, −LVdP/dt_{max} of H2 reversibly increased by 24%, 60% and 24%, respectively. In the presence of the β-blocker metoprolol (2.8 μmol/l, n = 5), these positive inotropic effects were reversed, resulting in a pronounced decrease in contractility. High performance liquid chromatography of the CE of H1 revealed an ischemia-induced time-dependent release of C from isolated hearts: After 10 min of IS no C were detected in the CE. In contrast, after 30 min of IS the concentration of C in the CE increased within 30 s to 8104 ± 324 pg/ml.

Conclusion: Cardiodepressive mediators are released from postischemic myocardial tissue during reperfusion. After prolonged IS (30 min) these cardiodepressive effects are counteracted by catecholamines.

990-35 A Comparative Study of Troponin I and Troponin T Release in Acute Myocardial Infarction

B.U. Goldmann, C. Heeschen, R.H. Möller, C.W. Hamm. *University Hospital Eppendorf, Dept. of Cardiology, Hamburg, Germany*

In acute myocardial infarction (AMI) troponin T (TnT) (31 kD) and troponin I (TnI) (22.5 kD) are released into circulation and represent highly specific markers for myocardial cell damage. Differences in release kinetics with relevance to clinical diagnostics have been so far unknown. In this study a newly developed one step solid phase enzyme immunoassay (EIA) with highly specific monoclonal antibodies for TnI measurement (cut-off 0.1 ng/ml) in AMI was compared with the TnT ELISA (cut-off 0.1 ng/ml). In n = 141 patients (pts) with confirmed AMI serum TnI and TnT measurements were performed at admission (3 ± 2 hours (hrs) after onset of symptoms) and after a 4 hrs interval. *Results:*

AMI n = 141 pts	TnT ≥ 0.1 ng/ml	TnI ≥ 0.1 ng/ml	p value
Admission	n = 94 (67%)	n = 109 (77%)	0.046
+ 4 hrs interval	n = 125 (89%)	n = 137 (97%)	0.005

Serum levels at admission (+4 hrs) were 0.6 ± 1.3 (5.9 ± 12.8) ng/ml for TnT and 1.7 ± 2.0 (12.7 ± 27.4) ng/ml for TnI. TnI increased earlier than TnT and revealed a higher diagnostic sensitivity for AMI.

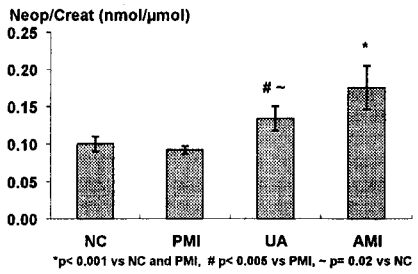
Conclusion: Based on these quantitative assays TnI was the superior marker for the early biochemical detection of AMI. The potential advantage of TnI as a serodiagnostic tool for therapeutic management of patients presenting with early onset of AMI deserves further clinical evaluation.

990-36 Neopterin, a Serum Marker of Immune Activation, is Elevated in Acute Coronary Syndromes

S. Gupta, S. Fredericks, R.A. Schwartzman, E.W. Leatham, M. Mendall, R. Crook, N. Ireson, J. Morris, D.W. Holt, J.C. Kaski. *St George's Hospital, London, UK*

There is growing evidence for an immunological basis for the pathophysiology of acute coronary syndromes. Neopterin is a sensitive serum marker for the activation of the cellular immune system. The relative activity of neopterin in acute and chronic ischaemic heart disease (IHD) was investigated in this study. Neopterin was measured by ELISA in the serum from 87 male cardiac patients. These included those with acute myocardial infarction (group AMI, n = 10), previous myocardial infarction (>6 months previously, group PMI, n = 60) and unstable angina (group UA, n = 17). Neopterin levels were also measured in a matched control group (NC, n = 42) with no evidence of IHD. Results are expressed as neopterin/creatinine ratios (mean ± SEM), correcting for renal function in all subjects.

Serum neopterin was significantly elevated in both the UA and AMI groups compared to PMI and NC groups. There was no difference in levels between UA vs AMI or PMI vs NC. *Conclusion:* The study findings support the evidence for the role of the cellular immune system in the pathophysiology of acute coronary syndromes.



990-37 The participation of Fas/Fas ligand system in apoptosis of cardiomyocytes in human acute myocardial infarction

T. Shimojo[1,2], T. Nishikawa[1], S. Ishiyama[1,2], H. Ito[2], T. Kasajima[1], F. Marumo[2], M. Hiroe[2]. *(1)Tokyo Women's Medical College, Tokyo, Japan, (2)Tokyo Medical and Dental University, Tokyo, Japan*

There are two types of cell death, necrosis, and apoptosis. It was reported that apoptosis occurs in cardiomyocytes by hypoxia and ischemia, and in acute myocardial infarction (AMI), concomitant with necrotic myocyte cell death. However, the molecular mechanism of the apoptotic cell death is remains unclear in myocardial ischemia and infarction. The Fas molecule is a tumor necrotic factor receptor family protein and produces a signal for apoptosis induction after binding to Fas ligand (L). In the present study, we investigated whether the Fas/Fas L system is associated with apoptotic cell death of hearts following AMI. Left ventricular specimens obtained from 10 patients died of AMI were used for detection of apoptosis using agarose-gell electrophoresis and the terminal deoxynucleotidyl transferase assay (TUNEL). Moreover, the expression of Fas and Fas L proteins, and T lymphocyte surface markers was examined by immunohistochemistry. Nuclear DNA electrophoretic analysis confirmed nucleosomal ladders in the affected area. The TUNEL positive cells were observed in the numerous cardiomyocytes and lymphocytes of the periinfarcted area, but not in the non-infarct myocardium. Immunohistochemical study showed strongly positive staining for Fas in the myocytes facing to the infarct and infiltrating lymphocytes. Fas L positive lymphocytes were classified as $CD4^+$ and $CD8^+$ T cells. These results incidate that Fas/Fas ligand system participates in apoptosis in human myocardium in AMI. These results suggest that the Fas/Fas L system is related to apoptotic cell death as a mechanism of cardiac injury following AMI.

991 Myocardial Infarction: Risk Stratification

Tuesday, March 18, 1997, Noon–2:00 p.m.
Anaheim Convention Center, Hall E
Presentation Hour: 1:00 p.m.–2:00 p.m.

991-13 Early Combined Electrocardiographic and Biochemical Risk Stratification of Patients with Unstable Coronary Artery Disease – A TRIM Substudy

L. Holmvang, M. Lüscher, K. Thygesen, G. Wagner, P. Grande. *The Heart Center, The National University Hospital, Copenhagen, Denmark, Department of Cardiology, Aarhus Amtssygehus, Aarhus, Denmark*

The present study investigates, whether the combination of a standard ECG and very early measurements of new, biochemical markers of ischemia could improve the identification of a high risk population in patients admitted with unstable coronary artery disease, ie non-Q MI or unstable angina. *Methods:* 516 patients were included. *Electrocardiographic analysis:* All patients had an ECG obtained at admission. The patients were divided into two subgroups based on whether they had significant ST-segment depression or not. *Biochemical analysis:* At admission and 6 hours later blood samples were drawn and analyzed for myoglobin, Troponin T (TnT), Troponin I (TnI) and CK-MB mass concentration. *Endpoints:* Death, myocardial infarction or refractory angina leading to acute intervention during a 30 days follow-up period. *Results:* The predictive value of ST-depression in the baseline ECG was 0.24. Only Myoglobin and TnT were increased among the patients suffering an event. Cut-off values for identifying a high risk patient were set at 0.1 μg/L (TnT) and 80 μg/L (Myoglobin).

TUESDAY POSTER